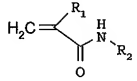
**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

1. (Currently Amended) A pharmaceutical composition having an anti-tumor effect comprising a pharmaceutically acceptable carrier or excipient and, as active ingredient,

- ~~an acryloyl distamycin derivative~~ a compound of formula (I):

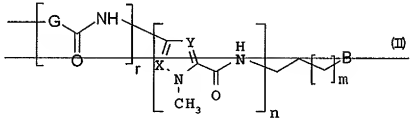


(I)

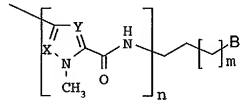
wherein:

$R_1$ is a bromine or chlorine atom;

$R_2$ is a group of formula (II)



(II)



(II)

wherein

m is ~~an integer from 0 to 2~~ 0 or 1;

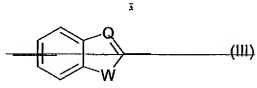
n is ~~an integer from 2 to 5~~ 3 or 4;

~~r is 0 or 1;~~

X and Y are, the same or different and independently for each heterocyclic ring, a nitrogen atom or a CH group;

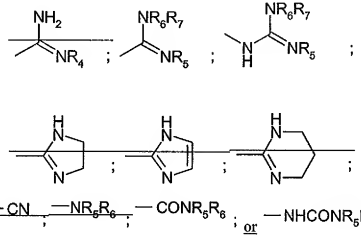
~~G is phenylene, a 5 or 6 membered saturated or unsaturated heterocyclic ring with from 1 to~~

~~3 heteroatoms selected among N, O or S, or it is a group of formula (III) below:~~




~~wherein Q is a nitrogen atom or a CH group and W is an oxygen or sulfur atom or it is a group $NR_3$ wherein $R_3$ is hydrogen or $C_1$-$C_4$ alkyl;~~

B is selected from the group consisting of



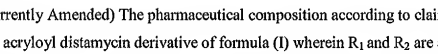

wherein ~~$R_4$ is cyano, amino, hydroxy or $C_1$-$C_4$ alkoxy;~~ $R_5$, $R_6$ and $R_7$, ~~the same or different,~~ are hydrogen ~~or $C_1$-$C_4$ alkyl; or a pharmaceutically acceptable salt thereof;~~ and

a protein kinase inhibitor; wherein said pharmaceutical composition has an antitumoral effect; and wherein said protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-)[[,]] and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-), ~~PKI166(Phenol, 4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-), EKB-569(2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-3-cyano-7-ethoxy-6-quinolinyl]-4-(dimethylamino)-,(2E)-), GW572016(4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-), CEP-2563(β-Alanine, L-lysyl-,[(9S,10S,12R)-2,3,9,10,11,12-hexahydro-10-methoxy-9-methyl-1-oxo-9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin-10-yl]methyl ester, hydrochloride (1:2)), UCN-01(9,13-Epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-1-one,2,3,10,11,12,13-hexahydro-3-hydroxy-10-methoxy-~~

~~9-methyl-11-(methylamino)-,(3R,9S,10R,11R,13R)-),~~ ~~[[G]]CGP 41251(Benzamide, N-[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methyl-), Safingol(1,3-Octadecanediol, 2-amino-, (2S, 3S)-), Perifosine(Piperidinium, 4-[[hydroxy(octadecyloxy)phosphinyl]oxy]-1,1-dimethyl-, inner salt), SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-), CGP 79787(1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-), ZD 6474(4-Quinazolinamine, N-(4-bromo-2-fluorophenyl)-6-methoxyl-7-[(1-methyl-4-piperidinyl)methoxyl]-), SU-11248(Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoror-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (1:1)), and Flavopiridol(4H-1-Benzopyran-4-one, 2-(2-chlorophenyl)-5,7-dihydroxy-8-[(3S,4R)-3-hydroxy-1-methyl-4-piperidinyl]-)~~; and the tumor to which the pharmaceutical composition has an anti-tumor effect is breast, lung, ovary, lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumor where the antitumoral effect of said pharmaceutical composition is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

2.-4. (Cancelled)

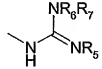
5. (Currently Amended) The pharmaceutical composition according to claim 1 comprising an acryloyl distamycin derivative of formula (I) wherein $R_1$ and $R_2$ are as defined in claim 1, ~~r is 0,~~ m is 0 or 1, n is 4, and X and Y are both CH groups ~~and B is selected from:~~




~~— CN ; — $CONR_5R_6$ ; — $NHCONR_5R_6$~~

~~wherein $R_4$ is cyano or hydroxy and $R_5$, $R_6$ and $R_7$, the same or different, are hydrogen or $C_1$-$C_4$ alkyl~~.

6. (Currently Amended) The pharmaceutical composition according to claim 5 comprising an acryloyl distamycin derivative of formula (I) wherein $R_1$ is bromine, $R_2$ is a group of formula (II) wherein ~~r and~~ m [[are]] is 0, n is 4, X and Y are CH, B is a group of formula



wherein $R_5$, $R_6$ and $R_7$ are hydrogen atoms, optionally in the form of a pharmaceutically acceptable salt.

7. (Previously Presented) The pharmaceutical composition according to claim 1 comprising an acryloyl distamycin derivative, optionally in the form of a pharmaceutically acceptable salt, selected from the group consisting of:

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}propyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-imidazole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-3-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrazole-5-carboxamide hydrochloride;

N-(5-{[(5-{[(5-{[(3-amino-3-oxopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-3-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrazole-5-carboxamide;

N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-chloroacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

N-(5-{[(5-{[(3-{[amino(imino)methyl]amino}propyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride;

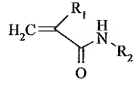
N-(5-{[(5-{[(3-amino-3-iminopropyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride; and

N-{5-[({5-[({5-[({3-[(aminocarbonyl)amino]propyl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}amino)carbonyl]-1-methyl-1H-pyrrol-3-yl}-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide.

8. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and, as active ingredient,

- N-(5-{[(5-{[(5-{[(2-{[amino(imino)methyl]amino}ethyl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)amino]carbonyl}-1-methyl-1H-pyrrol-3-yl)-4-[(2-bromoacryloyl)amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin); and
- a protein kinase inhibitor selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-), ~~and SU-5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-)~~; wherein the pharmaceutical composition has an antitumoral effect which is enhanced relative to the additive antitumoral effect of the Brostallicin and the protein kinase inhibitor.

9. (Currently Amended) A product comprising ~~an acryloyl distamycin derivative~~ a compound of formula (I):

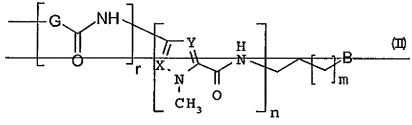


(I)

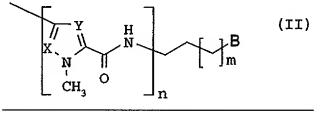
wherein:

$R_1$ is a bromine or chlorine atom;

$R_2$ is a group of formula (II)



(II)



(II)

wherein

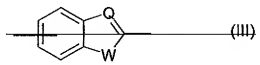
m is ~~an integer from 0 to 2~~ 0 or 1;

n is ~~an integer from 2 to 5~~;

~~r is 0 or 1;~~

X and Y are, the same or different and independently for each heterocyclic ring, a nitrogen atom or a CH group;

~~G is phenylene, a 5 or 6 membered saturated or unsaturated heterocyclic ring with from 1 to 3 heteroatoms selected among N, O or S, or it is a group of formula (III) below:~~

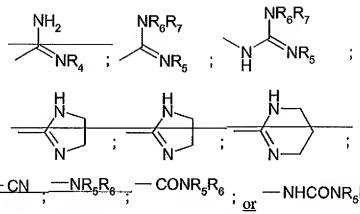


(III)

~~wherein Q is a nitrogen atom or a CH group and W is an oxygen or sulfur atom or it is a group $NR_3$~~

~~wherein $R_3$ is hydrogen or $C_1$-$C_4$ alkyl;~~

B is selected from the group consisting of




wherein ~~$R_4$ is cyano, amino, hydroxy or $C_1$-$C_4$ alkoxy;~~ $R_5$, $R_6$ and $R_7$, the same or different, are hydrogen ~~or $C_1$-$C_4$ alkyl;~~

or a pharmaceutically acceptable salt thereof; and

a protein kinase inhibitor, as a preparation where the acryloyl distamycin derivative may be administered simultaneously with the protein kinase inhibitor or, alternatively, both compounds may be administered sequentially in either order in the treatment of tumors; and wherein said protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-[[,]] and OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)~~-), PKI 166(Phenol, 4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-), EKB-569(2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-3-cyano-7-ethoxy-6-quinolinyl]-4-(dimethylamino)-,(2E)-), GW572016(4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxyl]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-), CEP-2563(β-Alanine, L-lysyl-,[(9S,10S,12R)-2,3,9,10,11,12-hexahydro-10-methoxy-9-methyl-1-oxo-9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-l][1,6]benzodiazocin-10-yl]methyl ester, hydrochloride (1:2)), UCN-01(9,13-Epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-1-one,2,3,10,11,12,13-hexahydro-3-hydroxy-10-methoxy-9-methyl-11-(methylamino)-,(3R,9S,10R,11R,13R)-), [[G]]CGP 41251(Benzamide, N-[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methyl-), Safingol(1,3-~~

~~Octadecanediol, 2-amino-, (2S, 3S)-), Perifosine(Piperidinium, 4-[[hydroxy(octadecyloxy)phosphinyl]oxy]-1,1-dimethyl-, inner salt), SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-), CGP 79787(1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-), ZD 6474(4-Quinazolinamine, N-(4-bromo-2-fluorophenyl)-6-methoxyl-7-[(1-methyl-4-piperidinyl)methoxyl]-), SU-11248(Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoror-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (1:1)), and Flavopiridol(4H-1-Benzopyran-4-one, 2-(2-chlorophenyl)-5,7-dihydroxy-8-[(3S,4R)-3-hydroxy-1-methyl-4-piperidinyl]-);** wherein the product has an antitumoral effect on breast, ovary, lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumor, which effect is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

10.-12. (Cancelled)

13. (Currently Amended) The product according to claim 9 comprising an acryloyl distamycin derivative of formula (I) wherein $R_1$ is bromine, $R_2$ is a group of formula (II) wherein ~~r and~~ m [[are]] is 0, n is 4, X and Y are CH, B is a group of formula


wherein $R_5$, $R_6$ and $R_7$ are hydrogen, optionally in the form of a pharmaceutically acceptable salt.

14. (Previously Presented) The product according to claim 9 wherein the acryloyl distamycin derivative is selected from the group as defined in claim 7.

15. (Currently Amended) A product comprising the acryloyl distamycin derivative N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and a protein kinase inhibitor selected from the group consisting of

STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-); as a combined preparation for simultaneous, separate or sequential use in the treatment of tumors, wherein said tumors are breast, ovary, lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumors.

16.-23. (Cancelled)

24. (Currently Amended) A method of treating a tumor selected from breast, ovary, lung, colon, kidney, stomach, pancreas or liver, cancer, melanoma, leukemia and brain tumor in a mammal, ~~suffering from~~ a ~~neoplastic disease state,~~ which method comprises administering to said mammal the acryloyl distamycin derivative of formula (I), as defined in claim 1, a and a protein kinase inhibitor selected from ST 1571 and OSI-774, in amounts effective to produce an antitumoral effect which is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

25. (Previously Presented) The method according to claim 24 wherein the acryloyl distamycin derivative is N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and the protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-).

26. (Currently Amended) The method for lowering the side effects caused by antineoplastic therapy with an antineoplastic agent, in a mammal in need thereof, the method comprising administering to said mammal a combined preparation comprising a protein kinase inhibitor and ~~an acryloyl distamycin derivative~~ a compound of formula (I), as defined in claim 1, in amounts effective to produce an antitumoral effect on tumors selected from breast, ovary,

lung, colon, kidney, stomach, pancreas, liver, melanoma, leukemia and brain tumors which is enhanced relative to the additive antitumoral effect of the acryloyl distamycin derivative and the protein kinase inhibitor.

27. (Currently Amended) The method according to claim 26 wherein the ~~acryloyl distamycin derivative~~ compound of formula I is N-[5-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-4-[[[4-[(2-bromo-1-oxo-2-propenyl)amino]-1-methyl-1H-pyrrol-2-yl[carbonyl]amino]-1-methyl-1H-pyrrole-2-carboxamide hydrochloride (Brostallicin), and the protein kinase inhibitor is selected from the group consisting of STI571(Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-), OSI-774(4-Quinazolinamine, N-(3-ethynylphenyl)-6, 7-bis(2-methoxyethoxy)-) and SU 5416(2H-indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1, 3-dihydro-).

28.-30. (Cancelled)

31. (Previously Presented) The method of treating a mammal according to Claim 24 wherein the mammal is human.

32. (Previously Presented) The method for lowering the side effects according to Claim 26 wherein the mammal is human.

33.-34. (Cancelled)